

REMARKS

At the outset, Applicants' representatives, Nikolaos C. George and Jennifer J. Chheda, thank Examiners Srivastava and Gitomer for giving us the opportunity to introduce ourselves.

A final Office Action was mailed July 13, 2004 in connection with the present application. Applicants' representatives filed in the United States Patent and Trademark Office ("USPTO") on January 12, 2005 a Notice of Appeal from the Examiner to the Board of Patent Appeals and Interferences and a Petition for Extension of Time for three (3) months. This Amendment, which is responsive to the July 13, 2004 final Office Action, is being filed in the USPTO with a Request for Continued Examination Under 37 C.F.R. § 1.114, a Petition for Extension of Time for two (2) months, a Supplemental Information Disclosure Statement and revised PTO-1449 form with copies of references B01-B29 and C01-C53.

Claims 1-21 were pending in this application. Applicants have canceled claims 1-21, without prejudice to Applicants' right to pursue the subject matter of the canceled claims in related applications. Applicants have added new claims 22-37 to more particularly point out and distinctly claim that which Applicants regard as their invention. New independent claims 22 and 23 (and claims 24-37 dependent therefrom) recite methods for treating or preventing colon cancer by administering to a human subject in need thereof a composition comprising specific polymethoxylated flavones. The polymethoxylated flavones recited in the pending claims are fully described in the specification (see, *e.g.*, the specification at page 4, lines 16-26). The names of some of the polymethoxylated flavones recited in the claims have been changed so that they more accurately reflect the systematic chemical name. Applicants respectfully assert that one of skill in the art would understand that the chemical names of the polymethoxylated flavones recited in the claims have the same structures as the polymethoxylated flavones recited in the specification. Support for the new claims can be found throughout the specification as filed, see, *e.g.*, page 3, lines 6-9, page 4, line 14 to page 7, line 21, page 8, lines 9-14, page 9, lines 8-31, page 10, lines 1-5, and page 11, lines 9-21 of the specification. Upon entry of this Amendment, claims 22-37 will be pending in this application.

Entry of the foregoing amendments and consideration of these remarks are respectfully requested.

**1. THE OBJECTIONS TO THE CLAIMS
SHOULD BE WITHDRAWN**

Claims 3, 4, 7-9, 11 and 13-16 are objected to for various reasons. In order to expedite prosecution and without conceding to the propriety of the objections, Applicants have canceled claims 3, 4, 7-9, 11 and 13-16, without prejudice. Thus, the objections to claims 3, 4, 7-9, 11 and 13-16 are moot and cannot stand. Accordingly, Applicants respectfully request withdrawal of the objections.

**2. THE REJECTION UNDER 35 U.S.C. § 112,
FIRST PARAGRAPH, SHOULD BE WITHDRAWN**

Claims 3-21 are rejected under 35 U.S.C. § 112, first paragraph, as not enabled for their full scope by the specification. Applicants acknowledge that the Examiner recognizes that the specification enables, *inter alia*, a method to treat cancer via administering a composition containing the 14 recited orange peel flavone components. (July 13, 2005 Office Action, page 3, paragraph 8).

In order to expedite prosecution and without conceding to the propriety of the rejection, claims 3-21 have been canceled, without prejudice. Thus, the rejection of claims 3-21 under 35 U.S.C. § 112, first paragraph, is moot and cannot stand. Accordingly, Applicants respectfully request withdrawal of the rejection.

Applicants have added new claims 22-37, directed to methods for treating and preventing colon cancer in a human. New independent claim 22 recites a method for treating colon cancer in a human comprising administering to a human in need of such treatment an effective amount of a composition comprising 14 specific polymethoxylated flavones, such that the colon cancer is treated. New independent claim 23 recites a method for preventing colon cancer in a human, the method comprising administering to a human in need of such prevention an effective amount of a composition comprising 14 specific polymethoxylated flavones, such that the cancer is prevented. Dependent claim 24 specifies that the method of preventing colon cancer recited in claim 23 results in a reduction in the presence of aberrant crypt or aberrant crypt foci. Dependent claims 25-36 specify the type or form of the composition administered to the human subject, or the amount of the composition administered to the human subject. Dependent claim 37 recites that the method for preventing or treating colon cancer further comprises administering to the human subject resveratrol, hydroxylated analogs of resveratrol, methoxylated analogs of resveratrol, a rosemary extract, a black tea extract, a Mexican Bamboo extract or a Huzhnag extract.

Applicants respectfully assert that the specification coupled with information known to the skilled artisan as of the effective filing date of the present application would have provided sufficient guidance to enable one of skill in the art to practice the claimed invention without undue experimentation.

The specification provides *in vitro* and *in vivo* assays for determining the efficacy of a composition comprising the specific polymethoxylated flavones recited in claims 22 and 23, alone or in combination with the extracts or compounds recited in claim 37, for the treatment and prevention of cancer (see, *e.g.*, page 4, line 27 to page 7, line 21 and page 8, line 17 to page 9, line 7). In addition, the specification provides *in vivo* data demonstrating that a composition comprising the specific polymethoxylated flavones recited in the pending claims is efficacious against colon cancer in an animal model for colon cancer as measured by a reduction in the formation of aberrant crypt, aberrant crypt foci, or the number colon tumors per mouse (see the specification at page 5, line 7 to page 7, line 21). The specification teaches that aberrant crypt and aberrant crypt foci are biomarkers for colon cancer and that these biomarkers have been utilized to assess prevention of colon cancer (see the specification at page 5, lines 23-25). Thus, a reduction in aberrant crypt or aberrant crypt foci demonstrates the efficacy of a composition comprising the specific polymethoxylated flavones recited in the pending claims in the prevention of colon cancer. Thus, the specification coupled with the information known as of the effective filing date of the present application have would have enabled one of skill in the art to practice the claimed methods of the invention without undue experimentation. Accordingly, Applicants submit that the pending claims are fully enabled for the scope of the claimed subject matter.

3. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the claimed invention.

Without acquiescing to the propriety of the rejection, Applicants point out that claims 1-21 have been canceled, without prejudice. Thus, the rejection of claims 1-21 under 35 U.S.C. § 112, second paragraph, is moot and cannot stand. Applicants further point out that new claims 22-37 contain none of the previously objected to terms. Accordingly, for the reasons set forth above, Applicants respectfully request withdrawal of the rejection.

**4. THE REJECTIONS UNDER 35 U.S.C. § 102
SHOULD BE WITHDRAWN**

Claims 1, 3, 5, 7, 8, 10 and 11 are rejected under 35 U.S.C. § 102(b) as anticipated by Attaway (Citrus Science and Properties. Food Phytochemicals for Cancer Prevention. ACS Symposia Series, 546, pp. 240-248) with evidence from Washino *et al.* (U.S. Patent No. 5,580,545) and Plant Specimen (<http://www.crescentbloom.com/Specimen/CI/default.htm>). Claim 12 is rejected under 35 U.S.C. § 102(b) as anticipated by Washino *et al.* with evidence from Plant Specimen.

In order to expedite prosecution and without conceding to the propriety of the rejections, claims 1, 3, 5, 7, 8, and 10-12 have been canceled, without prejudice. Thus, the rejections of claims 1, 3, 5, 7, 8, and 10-12 under 35 U.S.C. § 102(b) are moot and cannot stand. Accordingly, Applicants respectfully request withdrawal of the rejections.

**5. THE REJECTIONS UNDER 35 U.S.C. § 103(a)
SHOULD BE WITHDRAWN**

Claims 1-11 are rejected under 35 U.S.C. § 103(a) as obvious over Attaway with evidence from Washino *et al.* and Plant Specimen in view of Thomas *et al.* (U.S. Patent No. 5,830,738), Peirce (The American Pharmaceutical Association Practical Guide to Natural Medicines, 1999, Stonesong Press, Inc. pp. 563-566), Madis Botanicals (Madis Botanicals, Inc., Resverapure™ Resveratrol PE 8%, Product Code 04544, page 2, lines 6-7 and 15-31, 1997), Castleman (The Healing Herbs, The Ultimate Guide to the Curative Power of Nature's Medicine, 1991, Rodale Press, Emmaus, PA., page 349, column 2, lines 3-10) and Bailey *et al.* (U.S. Patent No. 5,829,293). Claims 12-21 are rejected under 35 U.S.C. § 103(a) as obvious over Washino *et al.* with evidence from Plant Specimen in view of Attaway and further in view of Thomas *et al.*, Peirce, Madis Botanicals, Castleman and Bailey *et al.*

In order to expedite prosecution and without conceding to the propriety of the rejections, claims 1-21 have been canceled, without prejudice. Thus, the rejections of claims 1-21 under 35 U.S.C. § 103(a) are moot and cannot stand. Accordingly, Applicants respectfully request withdrawal of the rejections.

Moreover, as discussed above, new independent claims 22 and 23 are directed to methods of treating and preventing colon cancer, respectively, in a human subject, comprising administering to a human in need thereof an effective amount of a composition comprising the specifically recited polymethoxylated flavones. Claims 24-37 ultimately depend from claim 22 and/or claim 23.

None of the cited references teach or suggest the currently claimed methods. Neither Attaway nor Washino *et al.* teach or suggest methods of preventing or treating colon cancer in a human subject by administering to a human in need thereof an effective amount of a composition comprising the polymethoxylated flavones recited in claims 22 and 23. Further, neither of these references teaches or suggests methods of preventing or treating colon cancer in a human subject by administering to a human in need thereof an effective amount of a composition comprising the polymethoxylated flavones recited in claims 22 and 23, in combination with resveratrol, hydroxylated analogs of resveratrol, methoxylated analogs of resveratrol, a rosemary extract, a black tea extract, a Mexican Bamboo extract or a Huzhnag extract.

The deficiencies in Attaway and Washino *et al.* are not cured by Thomas *et al.*, Bailey *et al.*, Peirce, Madis Botanicals, or Castleman, either alone or in combination. In particular, none of the references, either alone or in combination, teaches or suggests methods of preventing or treating colon cancer in a human subject by administering to a human in need thereof an effective amount of a composition comprising the polymethoxylated flavones recited in claims 22 and 23, alone or in combination with the extracts or compounds recited in claim 37.

Accordingly, Applicants submit that the cited references do not render the pending claims obvious.

CONCLUSION

Applicants believe that the present claims meet all the requirements for patentability. Entry of the foregoing amendments and remarks into the file of the application is respectfully requested. Withdrawal of all rejections and consideration of the amended claims are requested.

If any issues remain, the Examiner is urged to telephone the undersigned.

Respectfully submitted,

Date: May 11, 2005

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